Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 635-639 | ISSN:2251-6727

Role of Nanotechnology in Targeted Drug Delivery System: A Comprehensive Review

Mr. Abhay Kumar Dubey[1], Dr. Virendra Singh[2]

Mr. Abhay Kumar Dubey, Assistant Professor, Department of Pharmaceutics, Sainik Pharmacy College, Prayagraj 221505

Dr. Virendra Singh, Professor, Department of Pharmaceutical Chemistry, Sainik Pharmacy College, Prayagraj 221505

*** Corresponding Author**: Mr. Abhay Kumar Dubey,

(Received: 14 April 2024 Revised: 1 May 2024 Accepted: 18 June 2024)

KEYWORDS

Nanotechnology, Active and Passive targeting, Nanoparticles.

ABSTRACT:

Nanotechnology, a rapidly advancing field, involves developing materials with sizes between 5-200 nanometres. In medicine, nanotechnology has shown significant potential in drug delivery and treatment for various diseases. Biodegradable nanoparticles are designed to encapsulate drugs, protecting them from degradation and ensuring targeted delivery. This approach enables precise dosing and site-specific action, reducing side effects by depositing the active agent only in the affected area. Various materials, including proteins, polysaccharides, and synthetic polymers, are used to prepare nanoparticles, considering factors like size, drug properties, surface characteristics, and biodegradability. Gold nanoparticles have shown promise in cancer therapy, while solid lipid nanoparticles have demonstrated efficacy in anti-cancer and antiviral treatments. Other nanotechnology-based drug delivery systems, such as nanofibers and nanosuspensions, are also being explored. The application of nanotechnology has revolutionized drug delivery, enabling precise and targeted administration of therapeutic agents.

Introduction

Nanotechnology may be defined as science which involves design characterization, production and application of device system and methodology to control the size and shape to nano range. Nanotechnology has great role in pharmaceutical drug delivery system in improvement of newer formulations for diagnosis, prevention, and treatment of various kind of disease(1). Nanotechnology helps to improve wide range of formulations for drug delivery system, drug targeting, to improve technique drug delivery techniques, enhance the efficacy of drug as well as to reduce to toxicity and amount of drug required to produce effect(2).

Researchers have made significant progress in developing drug delivery systems that target specific cells. Nanotechnology has emerged as a promising approach, utilizing nanoparticles as drug carriers. These tiny particles, composed of polymers and lipids, exhibit distinct physical and biological properties due to their miniature size. This unique profile makes them an attractive tool for biomedical applications, enabling both systemic and localized treatment options(3).

When developing targeted therapies, the method of attaching drugs to carriers and the targeting strategy are crucial. Nanocarriers can either adsorb or covalently bind to drugs, with covalent linking offering the advantage of controlled drug loading. An ideal nanoparticle drug carrier must be biodegradable, biocompatible, non-toxic, and suitable for human use. Both active and passive mechanisms can achieve cell-specific targeting with nanocarriers. Active targeting employs recognition ligands or low molecular weight ligands, such as fatty acids or peptides, to guide the drug-nanocarrier conjugate to the affected site. Active targeting can also be achieved through manipulation of physical conditions like temperature or pH. In contrast, passive targeting relies on the enhanced permeability and retention (EPR) effect in leaky tumor tissues. Once

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 635-639 | ISSN:2251-6727

the drug-nanocarrier conjugate reaches the diseased tissue, the therapeutic cargo is released. Nanocarriers can also release drugs in response to changes in physiological conditions like temperature, pH, osmolality, or magnetism. These advancements have made nanomedicine a promising and exciting approach for treating a wide range of diseases(4).

Mechanisms of Nanoparticles as Targeting Drug Delivery System

The two mechanisms by which nanoparticles can attach to drugs and target diseased tissue are:

Active targeting: This involves attaching molecules to the nanoparticle surface that specifically bind to receptors or antigens on the surface of target cells, such as cancer cells. This helps the nanoparticle-drug complex to selectively target and accumulate at the disease site(5).

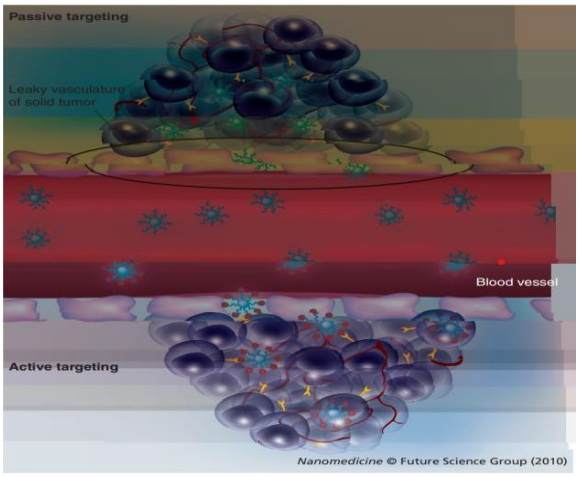

Figure 1: Active targeting and Passive targeting for drug delivery to solid tumors.

Passive targeting: This relies on the natural properties of nanoparticles, such as their small size and surface chemistry, to accumulate at the disease site through passive mechanisms like enhanced permeability and retention (EPR) effect. The EPR effect allows nanoparticles to leak out of blood vessels and accumulate in the tissue around the tumor, where they can release the drug(6).

Increased retention time and permeability: Nanoparticles that meet specific requirements, such as prolonged circulation in the bloodstream and enhanced targeting of tumor tissues, can effectively accumulate in tumor tissues. This is due to the distinct characteristics of tumor cells.. Rapidly growing cancer cells require new blood vessels to obtain oxygen and nutrients, leading to the formation of leaky and chaotic vasculature. This imperfect vascular architecture enables nanoparticles to penetrate and accumulate in tumor tissues, enhancing drug delivery and potential therapeutic efficacy.

Antigen expression. Ideally, cell-surface antigens and receptors should have several properties that render them particularly suitable tumor-specific targets. First, they should be expressed exclusively on tumor cells and not expressed on normal cells. Second, they should be expressed homogeneously on all targeted tumour cells. Last, cell-surface antigens and receptors should not be shed into the blood circulation.

Targeted conjugates internalization: a crucial factor in selecting appropriate targeting ligands. After binding to target cells, receptor-mediated endocytosis typically facilitates internalization. Using the folate receptor as an example, when a folate-targeted conjugate binds to the receptor on the cell surface, the plasma membrane invaginates, forming an endosome that encapsulates the receptor-ligand complex. The newly formed endosome is then transported to target organelles, where the acidic pH and activated lysozymes trigger the release of the drug from the conjugate. The drug then enters the cytoplasm, provided it has the necessary physicochemical properties to cross the endosomal membrane. The released drug is then trafficked to its target organelle, depending on its specific properties. Meanwhile, the folate receptor, now free from the conjugate, returns to the cell membrane, ready to initiate another round of transport by binding with new folate-targeted conjugates.

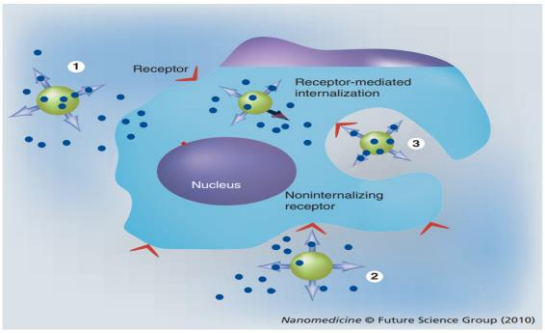

Figure 2. Mechanism of the drug release when reaching the tumor site(7).

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 635-639 | ISSN:2251-6727

Types of Nanoparticles

Liposomes: The term liposome is derived from the Greek words "lipo" meaning fat and "soma" meaning body, aptly describing its composition of phospholipids. As the first drug carriers to be investigated, liposomes are colloidal particles typically ranging from 80-300 nm in size. Phospholipids like phosphotidylglycerol and phosphatidic choline are the main constituents of liposomes, as discussed by Moussaoui et al. (2002) and Banerjee R. (2001). The properties and characteristics of liposomes depend on factors like lipid choice, size, composition, and preparation method. Lipids are also used to formulate solid lipid nanoparticles (SLNs) and nanocapsules. Liposomes have shown great promise in drug delivery, enhancing solubility, pharmacokinetic properties, and therapeutic index while reducing side effects(8). Modified liposomes, such as multifunctional liposomes containing specific proteins or antigens, can be designed for targeted drug delivery. In recent years, several liposomal drug delivery systems have been approved, with others in clinical trials(9).

Nanocrystals: Nanocrystals are molecular aggregates that can form crystalline structures. While they have extensive applications in chemical and biological engineering, their use in nanomedicine for drug delivery is relatively limited. However, nanocrystals can be modified by coating hydrophobic compounds with a hydrophilic layer, which affects their reactivity. The combination of these factors makes nanocrystals a promising tool for drug delivery systems, offering potential benefits such as improved solubility and targeted release(10).

Nanorobotics: It involves designing and building microscopic machines, typically measuring between 0.1-10 micrometers, composed of nanoscale or molecular components. This emerging field has vast potential in medicine, including early cancer diagnosis, targeted drug delivery, biomedical instrumentation, surgery, pharmacokinetics monitoring for diabetes, and overall healthcare. Future medical nanotechnology may employ nanorobots that operate at a cellular level, injected into patients to perform specific tasks. These medical nanorobots should be designed to be non-replicating to ensure reliability and focus on their medical mission. Instead, they would be manufactured in controlled nanofactories, integrating nanoscale machines into desktop-scale devices that produce macroscopic products. Robert Freitas has presented detailed theoretical discussions on nanorobotics in the context of nanomedicine, addressing design issues like sensing, power, communication, navigation, manipulation, locomotion, and onboard computation. However, some of these discussions remain theoretical and require further engineering development to become practical realities(11).

Polymeric nanoparticles: Polymeric nanoparticles, ranging from 10-100nm in size, can be prepared from both biodegradable and non-biodegradable materials. Their small size enables efficient cellular uptake, leading to increased drug accumulation at target sites. These nanoparticles can accommodate a wide range of hydrophobic and hydrophilic drugs. The polymeric material's functional groups can be modified with targeting ligands. Various methods can be employed to immobilize drugs in nanoparticles. The polymers PCL (Poly Caprolactone) and PLGA (PolyLactone-coglycoside) are notable examples, exhibiting efficient uptake by immune cells due to their hydrophobicity. These nanoparticles have been explored for various applications, including cancer asthma, tuberculosis, hypertension, oral delivery of insulin, and targeted drug delivery for Alzheimer's disease. To achieve targeted drug delivery, drugs are conjugated to cell-specific ligands that can reach specific organs. Drugs are incorporated into nanoparticles through dissolution, adsorption, or entrapment, enabling efficient release at targeted sites. The literature review highlights the potential of polymeric nanoparticles in drug delivery, demonstrating their efficiency and suitability for this application(12).

Biological Transport of Nanoparticles

For effective drug delivery, accessing target sites through microcirculation via blood capillaries or surface pores and membranes is crucial. The majority of openings and gates at cellular and subcellular levels are nanometer-sized, making nanoparticles ideal for reaching subcellular levels. A key requirement for any delivery system is the ability to move freely through available pathways and cross various barriers. In the human body, blood vessels are the primary transportation routes, branching into thinner capillaries that reach close to individual cells. After reaching their

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 635-639 | ISSN:2251-6727

smallest size, capillaries merge to form veins, which return contents to the heart for recirculation. To remain in the vasculature, a moiety must be narrower than the cross-sectional diameter of the narrowest capillaries (approximately 2000 nm). For efficient transport, nanoparticles should be smaller than 300 nm. However, mere vessel transport is insufficient for drug delivery; targeted release and absorption are also essential.

To effectively deliver drugs, the delivery system must overcome various barriers to reach the target site. This involves crossing the blood capillary wall to enter the extracellular fluid and potentially traversing additional cells to reach the target cell. Nanoparticles must navigate these obstacles during their journey through vessels and across barriers. There are two routes for crossing blood capillaries and cell layers: transcellular and paracellular. The transcellular route requires the nanoparticle to enter and exit cells to reach the tissue, surviving the intracellular environment. In contrast, the paracellular route allows nanoparticles to move between cells through intercellular junctions, avoiding cellular destruction. The paracellular movement of molecules, including ions and leukocytes, is regulated by tight junctions and adherence junctions. Tight junctions act as a regulated barrier, while adherence junctions develop and stabilize tight junctions. Different epithelial and endothelial barriers have varying permeabilities due to structural differences and tight junction presence. Epithelia and brain capillary endothelium exhibit high barrier function, while vascular endothelium in other tissues is more permeable. Tight junctions control paracellular transport, making them a crucial aspect of drug delivery.

Applications:

Nanotechnology in Cancer: The application of nanotechnology in cancer research has shown promising results. Scientists have utilized ethylene glycol to deliver therapeutic drugs to cancer cells, leveraging its ability to evade recognition by white blood cells and prolong circulation in the bloodstream, ultimately targeting cancer cells. Additionally, researchers at IBM have successfully demonstrated drug delivery using hydrogels. Ongoing research aims to enhance the efficacy of drug-carrying nanoparticles in penetrating tumors, further advancing cancer treatment.

Conclusion

The decision between active and passive tumor targeting should consider the characteristics of both the tumor cells and the drug. For drugs like doxorubicin that readily penetrate cells, encapsulation in stealth nano systems that rely on passive targeting is sufficient. Encapsulating these drugs in long-circulating stealth nanocarriers enhances their accumulation in tumor tissues, reducing toxicity to organs like the heart, kidneys, and liver. However, for therapeutic molecules with poor cell membrane permeability and potential toxicity to normal cells, active targeting is preferred. This involves decorating nanocarriers with ligands specific to receptors overexpressed on cancer cells. While active targeting is more efficient, the surface decoration process can be complex, especially for nano emulsions. In some cases, the strategy may prioritize simplicity, relying solely on the enhanced permeability and retention (EPR) effect without active targeting.

Future Aspect: Nanotechnology is a rapidly evolving field poised to transform drug delivery and revolutionize the treatment of various diseases. While nanotech in medicine promises significant advances, the complexity of manufacturing nanodrug delivery systems may present a challenge for pharmaceutical companies. To overcome this hurdle, experts from diverse fields must collaborate to translate innovative lab discoveries into commercially viable products. The ultimate objective of nanodrug delivery systems is to develop clinically effective formulations that can effectively treat a broad spectrum of diseases.

Bibliography

1. McNeil SE. Nanotechnology for the biologist. J Leukoc Biol. 2005 May 27;78(3):585–94.
2. Shivani S, Kumar Poladi K. NANOSPONGES-NOVEL EMERGING DRUG DELIVERY SYSTEM: A REVIEW. Int J Pharm Sci Res [Internet]. 2015;6(2):529. Available from: http://dx.doi.org/10.13040/IJPSR.0975-8232.6
3. Malik S, Muhammad K, Waheed Y. Nanotechnology: A Revolution in Modern Industry. Molecules. 2023 Jan 9;28(2):661.
4. Poole CP, Frank Owens JJ. INTRODUCTION TO NANOTECHNOLOGY @z+::iCIENcE zyxwvutsrqponmlkjihgfe [Internet]. 2003. Available from: www.copyright.com.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 635-639 | ISSN:2251-6727

5. Sato Y, Sakurai Y, Kajimoto K, Nakamura T, Yamada Y, Akita H, et al. Innovative Technologies in Nanomedicines: From Passive Targeting to Active Targeting/From Controlled Pharmacokinetics to Controlled Intracellular Pharmacokinetics. Macromol Biosci. 2017 Jan 31;17(1).
6. BAZAK R, HOURI M, ACHY S EL, HUSSEIN W, REFAAT T. Passive targeting of nanoparticles to cancer: A comprehensive review of the literature. Mol Clin Oncol. 2014 Nov;2(6):904–8.
7. Huynh NT, Roger E, Lautram N, Benoît JP, Passirani-Malleret C, Passirani C. The rise and rise of stealth nanocarriers for cancer therapy: passive versus active targeting. Nanomedicine [Internet]. 2010;5(9). Available from: https://univ-angers.hal.science/hal-03171842
8. Li Z, Liu M, Wang H, Du S. Increased cutaneous wound healing effect of biodegradable liposomes containing madecassoside: Preparation optimization, in vitro dermal permeation, and in vivo bioevaluation. Int J Nanomedicine. 2016;11:2995–3007.
9. Sapra P, Tyagi P, Allen T. Ligand-Targeted Liposomes for Cancer Treatment. Curr Drug Deliv. 2005;2(4):369–81.
10. Lu Y, Li Y, Wu W. Injected nanocrystals for targeted drug delivery. Acta Pharm Sin B. 2016 Mar;6(2):106–13.
11. Kasabov N, Havukkala I. <I>A Special Issue on</I> Computational Intelligence for Bioinformatics. J Comput Theor Nanosci. 2005 Dec 1;2(4):471–2.
12. V N NB, Ksyadav H. DIFFERENT TECHNIQUES FOR PREPARATION OF POLYMERIC NANOPARTICLES-A REVIEW.